CLAIMS

1. A sustained release preparation comprising a combination of a microcapsule which gradually releases a GnRH agonist or a salt thereof for a long term, and a microcapsule which gradually releases a GnRH agonist or a salt thereof for a short term.

2. The preparation according to claim 1, wherein the GnRH agonist or a salt thereof is a peptide represented by the formula:

5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z

[wherein Y represents a residue selected from DLeu, DAla, DTrp, DSer (tBu), D2Nal and DHis (ImBzl), and Z represents $NH-C_2H_5$ or $Gly-NH_2$]

or a salt thereof.

3. The preparation according to claim 1, wherein the GnRH agonist or a salt thereof is an acetate of a peptide of the formula:

5-oxo-Pro-His-Trp-Ser-Tyr-Dleu-Leu-Arg-Pro-$NH-C_2H_5$

4. The preparation according to claim 1, wherein the long term is 5 months or longer, and the short term is shorter than 5 months.

5. The preparation according to claim 1, wherein the long term is 5 months or longer and 8 months or shorter, and the short term is 1 week or longer and shorter than 5 months.

6. The preparation according to claim 1, wherein the microcapsule is a microcapsule containing a lactic acid polymer or a lactic acid-glycolic acid polymer as a base.

7. The preparation according to claim 1, wherein a combination ratio of the microcapsule which gradually releases a GnRH agonist or a salt thereof for a short term to the microcapsule which gradually releases a GnRH agonist or a salt thereof for a long term is 1: about 5 to 1: about 20 expressed as a ratio of a weight of the GnRH agonist or a salt thereof contained in each microcapsule.

8. The preparation according to claim 1, wherein:

the microcapsule which gradually releases the GnRH agonist or a salt thereof for a long term is:

a microcapsule containing (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid polymer having a weight-average molecular weight of about 18,000 to about 30,000; and

the microcapsule which gradually releases a GnRH agonist or a salt thereof for a short term is:

(1) a microcapsule containing (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid-glycolic acid polymer (75/25 (mol%)) having a weight-average molecular weight of 8,000 to about 12,000, or

(2) a microcapsule containing (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid polymer having a weight-average molecular weight of about 13,000 to about 18,000.

9. The preparation according to claim 1, wherein:

the microcapsule which gradually releases a GnRH agonist or a salt thereof for a long term is:

a microcapsule containing (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid polymer having a weight-average molecular weight of about 15000 to about 50000 in which a content of a polymer having a weight-average molecular weight of 5000 or less is about 5% or less by weight; and

the microcapsule which gradually releases a GnRH agonist or a salt thereof for a short term is:

(1) a microcapsule which contains (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid-glycolic acid polymer in which a weight-average molecular weight (Mw) is about 8,000 to about 11,500, and a ratio of a weight-average molecular weight (Mw) to a number-average molecular weight (Mn) is greater than 1.9, and a compositional molar ratio

of lactic acid to glycolic acid is 99.9/0.1 to 60/40, and which does not contain a drug retaining substance, or

(2) a microcapsule which zero order-releases a GnRH agonist or a salt thereof over 2 months, and which is prepared by microencapsulating a W/O emulsion prepared from an inner aqueous phase solution containing a GnRH agonist or a salt thereof in about 20 to 70% by weight, and an oil phase solution containing, as a release controlling substance, a copolymer or a homopolymer in which a compositional ratio of lactic acid/glycolic acid is 80/20 to 100/0, and a weight-average molecular weight is about 7,000 to about 30,000.

10. The sustained-release preparation according to any one of claim 1 to 9, which gradually releases a GnRH agonist or a salt thereof for a long term.

11. The sustained-release preparation according to claim 10, wherein the long term is 5 months or longer.

12. An agent for preventing or treating prostate cancer, prostatomegaly, endometriosis, hysteromyoma, metrofibroma, precocious puberty, dysmenorrhea or breast cancer, or a contraceptive agent, comprising the sustained-release preparation according to claim 1.

13. A process for producing the sustained-release preparation according to claim 1, which comprises mixing a microcapsule which gradually releases a GnRH agonist or a salt thereof for a long term and a microcapsule which gradually releases a GnRH agonist or a salt thereof for a short term.

14. A method for preventing or treating prostate cancer, prostatomegaly, endometriosis, hysteromyoma, metrofibroma, precocious puberty, dysmenorrhea or breast cancer, or preventing conception, which comprises administering an effective amount of the sustained-release preparation according to claim 1 to a mammal.

15. Use of the sustained-release preparation according to claim 1 for producing an agent for preventing or treating prostate cancer, prostatomegaly, endometriosis, hysteromyoma, metrofibroma, precocious puberty, dysmenorrhea or breast cancer, or a contraceptive agent.